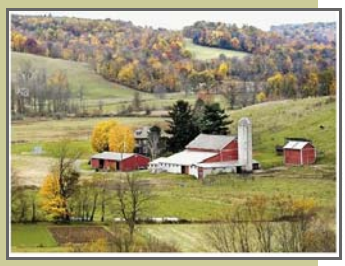

Bipolar Genetics

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People *who volunteer for our studies often ask us how the research is going. What have we found? Do I have the gene? What about my children? It can seem at times that the progress is slow, and that practical benefits are still a long way off. Here, Dr. Francis McMahon, Chief of the Human Genetics Branch at the National Institutes of Health, who leads the bipolar disorder genetics study, offers a progress report.*

What have we learned so far? We have been working with the Plain People in the Amish and Mennonite communities for about 2 years, but our genetic testing is still in the early stages. So far it looks like bipolar disorder among the Plain People is not very different from what we see so often in others:

- The illness often begins with a period of depression in the late teens or early twenties;
- 1 in 2 people with the illness end up being hospitalized for a severe manic episode;
- The average person stays in the hospital about 2 to 2 1/2 weeks.

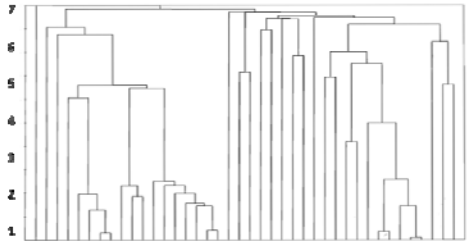
One important difference: Amish and Mennonite patients are less likely to report psychosis during their illness episodes, such as hearing voices. This might reflect the much lower rates of street drug use in Plain communities, since we know street drugs make bipolar disorder worse and increase the risk of psychosis.

Our genetic tests are not yet far enough along to pinpoint any particular genes that may play a role in bipolar disorder. So we can't yet identify adults or children who might be at a high risk for the illness. But the tests we've done so far do show that the Amish we've studied in Ohio, Indiana, and Pennsylvania are all somewhat related (see Box). The Amish in Pennsylvania seem to be a different group than those in Ohio and Indiana, but these two broad groups of people still appear to be distantly related. How related? This is hard to answer exactly, since people can be related in many ways. On average, the Amish in Pennsylvania are about 6 to 7 generations removed from those in Ohio and Indiana. Some people are more closely related, and some do not seem to be related at all.

Why are Amish and Mennonite Families so Important? Scientists who study inherited illnesses can learn a lot from families. Families are a kind of "natural laboratory" in which large numbers of genes get shuffled around from generation to generation. Just as important, relatives with similar genes, such as brothers and sisters, also tend to share similar life circumstances and experiences. So families are the real-life setting where genes interact with the environment to produce health or disease.

But big families are getting to be less and less common nowadays, especially in the United States. In some communities, large families are still a common part of life. The Amish and Mennonites are two such communities. They are also what geneticists call founder populations: Groups of people who can trace their families back to relatively few ancestors, and who have not married a lot of people from outside the community. Founder populations like these can be really helpful, because they may have fewer genes that contribute to any given disease. This might simplify the picture a bit for diseases like bipolar disorder that seem to be caused by many different genes in different people.

What's next? As we complete genome sequencing on more and more volunteers, we expect be begin to narrow down the list of genes that contribute to bipolar disorder. We don't expect to find just one, but a list of candidates might help us piece together a theory of what goes wrong in the brain when someone has bipolar disorder – and maybe, how we can better treat it.



Box. ***Overall genetic relationships among 40 Amish volunteers, based on genetic markers. Each person is represented by a vertical line. The number of generations of separation is shown on the far left. Volunteers from Ohio and Indiana (right) seem to form a distinct group, 6 to 7 generations removed from those in Pennsylvania (left).***

Bipolar Genetics

Recruitment in the Amish and Mennonite Communities:
How we started, where we are, and the future
Layla Kassem

Our research on the genetic basis of bipolar disorder started 25 years ago, and aimed at answering the following questions:
Is bipolar disorder an inherited disease? How is it inherited and what, if any, are the genes that place individuals at risk for developing the disorder?

Through studying families in many different communities in both America and other countries, we were able to determine that bipolar disorder is familial. What remains for us to determine is how it is familial, and to identify the biological and environmental factors that may place individuals in families at risk for developing this illness.

In order to answer these remaining questions we need the participation of many affected (ill) and healthy individuals and families from many communities. Our interest in working with the Amish and Mennonite communities started in 2009 when it became clear to us that some of the answers to our questions would be best addressed through working with large families who have clear genealogical information.

In the fall of 2009 after advertising our genetic study in "The Budget" we were invited to meet members of the Amish community in Ohio, that was our introduction, as well as the start of our work with the community. The first visit to the community in Berlin, OH was very productive and allowed our team to introduce itself and its work. It also allowed community members to teach our team about Amish life and traditions, and to ask questions and gain information about mental health and mental illness, specifically bipolar disorder. In addition to being introduced to the community and recruiting participants for the study, our visit to Ohio also resulted in an invitation to present our work at Oaklawn Hospital in June 2010. Our work was very well received by the community at Oaklawn and the Amish community in Indiana. Since then we have developed a relationship with Oaklawn, and we have recruited many families from Indiana and other states.

It was not until mid 2011 that our work was sufficiently established in and familiar to the community. Since then the number of families and individuals participating in this research has grown exponentially. At this time we have enrolled a total of 46 families. These families are from Indiana, Ohio, Pennsylvania, Southern Maryland and New York.

Our plan for the next few years is to continue with our recruitment of new families as well as following up with families already participating in this study. We will be expanding the geographic area we cover to include Illinois, Wisconsin, Missouri, Kansas, Wyoming, Delaware, Iowa, Florida and Canada. We aim to collect a large number of Amish and Mennonite families, and together we will contribute knowledge to the Amish and Mennonite communities and to the scientific community.

BIPOLAR *genetics*
You can participate in this research study if you are over 18, have a bipolar diagnosis, or have a family member with bipolar disorder. This study includes an interview (2-4 hours) and a blood sample (blood work from your physician.)
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human genetics

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